GENA SAARI WHITNEY

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PROFESSIONAL EXPERIENCE

BRISTOL-MYERS SQUIBB/PRI, Princeton, NJ 2002 to Present

Lawrenceville Discovery Biology/ Immunology
Immune Cell Function Group (2002-Present)
Sr. Research Scientist I
Supervisor: James Burke, Ph.D.

Member of a Full Program Discovery Working Group- Collaborated with the Applied Genomics group on two transcriptional profiling experiments to profile compounds. These two Transcriptional Profiling experiments provided valuable data for the DWG showing the effectiveness and lack of off-target activity of the compounds. Also Applied Genomics have used these experiments as an example of the usefulness of transcriptional profiling analysis. The blinded data have been presented at external meetings.

Currently responsible for screening program compounds in a promoter luciferase assay. Previously had been screening the compounds with a lactamase assay and Alamar Blue cytotoxity assay.

Previously, identified a COPD Exploratory target from collaboration with Proteomics group and was responsible for coordinating validation efforts across groups and sites an followed up on possible Oncology indication for RAI-3.

BRISTOL-MYERS SQUIBB/PRI, Princeton, NJ
Immunology, Inflammation and Pulmonary Disease Management Area 2000 to 2002
Pulmonary Focus Group (2000-Present)
Research Scientist I I
Supervisor: Murray McKinnon, Ph.D. Current position: Director, Immunology Discovery, Lawrenceville Biology

As a member of the Pulmonary Focus Group was responsible for Pulmonary Exploratory work, including asthma target validation and COPD target identification.

- Treated airway epithelial cells with cigarette smoke-bubbled RPMI and identified a dose and time point which gives a robust phosphotyrosine signal to be used in proteomics project.
- Airway epithelial cell/cigarette smoke-treated viability assays.
- Showed that the exploratory target, Siglec-10 could be tyrosine phophorylated by lck and JAK3 kinases.

- Showed that a phosphorylated GST fusion of Siglec-10 could fish out endogenous SHP-1 and SHP-2 from cell lysates.
- Constructed four GST-Siglec-10 cytoplasmic Y to F point mutants and identified which tyrosine(s) SHP-1 and SHP-2 bind to. Made GST fusion constructs of SHP-1 and SHP-2 tandem SH2 domains and showed direct binding of Siglec-10 Y667 phosphopeptide to GST SHP-1 and SHP-2.
- Determined the Siglec-10 gene structure from public genomic database contig.

BRISTOL-MYERS SQUIBB/PRI, Princeton, NJ
Signal Transduction Focus Group (1997-Present) 1997 to 2000
Research Scientist I I
Supervisor: Steven B. Kanner, Ph.D. Current position: Director, Preclinical Research, Agensys, Inc. Santa Monica, CA

As a member of the Signal Transduction department for over two years, was responsible for developing assays adaptable to a high through put screen for small molecular weight inhibitors of the SH2/phophotyrosine protein:protein interaction and identifying novel targets for drug discovery.

BRISTOL-MYERS SQUIBB/PRI, Seattle, WA 1991-1997
Immunological Diseases Therapeutic Area
Inflammation Department (1991-1997)
Research Scientist I
Supervisor: Alejandro Aruffo, Ph.D. Current position: President, Abbott Bioresearch Center and divisional Vice President, Abbott Laboratories. Worcester, MA.

As a member of the Inflammation department for six years, responsible for cloning and characterizing novel molecules expressed in the immune system. Attended Incyte database workshop and Yeast Two-Hybrid workshop.

- Molecular characterization CD5 cytoplasmic domain and identification of specific tyrosine responsible for SHP-1 SH2 binding.
- Analysis of the tyrosine phosphorylation and signal transduction of naturally occurring human CD6 isoforms with different cytoplasmc domains.
- Studied the role of CD6 in the regulation of the immune response- characterized the CD6 ligand binding domain by construction and expression of Ig fusion deletion mutants and identification of binding domain by FACs analysis and ELISAs. Isolated the mouse CD6 cDNA. Generated Ig fusions of deletion mutants of murine CD6 used to map epitopes of monoclonal antibodies.
- Analyzed CD6 intracellular domain- Identification of CD6 phosphotyrosines by site directed mutagenesis and generation of stable Jurkat cell lines, FACs analysis, IPs and P-Tyr blots. Used the yeast two-hybrid system in an attempt to isolate proteins interacting with CD6 intracellular domain. Characterized splice-variant isoforms of the cytoplasmic domain by mapping intron/exon boundaries, isolated human genomic clones and determined the CD6 gene structure.
- In addition,. cloned the human cDNA for Focal Adhesion Kinase by cross hybridization.

Isolated cDNAs and constructed soluble forms of the subunits to the LFA-1 and VLA-4 integrins. Isolated a cDNA by expression cloning that is phosphorylated in T cells following T cell activation.

BRISTOL-MYERS SQUIBB/PRI, Seattle, WA 1988-1991
Molecular Biology Department (1988 - 1991)
Associate Research Scientist
Supervisor: Greg Plowman, Ph.D., MD. Current position: Senior Vice President and Chief Scientific Officer, Exelixis Corp., So. San Francisco, CA

As a member of the Molecular Biology group for almost three years, responsible for isolating and characterizing novel growth factor receptors in the HER2/EGFR family.

- Screened cDNA libraries by cross-hybridization and used degenerate oligos for PCR on genomic DNA to obtain novel HER2/EGFR family members. Cloned HER3 and HER4.
- Generated constructs to characterize the novel receptors by analysis of chimeras with EGFR and constructs containing deletions or point mutants. Assayed for gene expression by PCR-based techniques, Northerns and Westerns.

UNIVERSITY OF ZURICH, Zurich, Switzerland 1986-1988
Zoological Institute (1986-1988)
Research Associate
Supervisor: Mariann Bienz, Ph.D. Current address: MRC Laboratory of Molecular Biology, Cambridge, England

Research Associate in a Drosophila lab, conducting research on the regulation of Drosophila homeotic genes.

- Identified transcript-positive regions by reverse Northerns using oligo-dT-primed, random-primed and specific oligo-primed probes, in particular, to identify 5' exons. Mapped 5' ends of transcripts by S1 mapping and primer extension with reverse transcriptase. Sequenced cDNAs and genomic regions of the bithorax and antennapedia complexes and analyzed data with Staden software. Mapped breakpoint of mutation within the bithorax complex by Southerns and then cloning and sequencing.
- Constructed promoter-lacZ fusions in vectors for P-element mediated integration into the germline of Drosophila embryos. Prepared embryos for injection of promoter-lacZ fusions. Isolated DNA from transformed lines, performed Southerns to confirm identity of integrated constructs. Assayed transformed embryos containing various constructs for total b-gal activity.
- Transformed Drosophila Schneider cells with promoter-lacZ and promoter-CAT fusions. Co-transformed cells with putative activator of promoter. Assayed cells for b-gal or CAT activity.

ZYMOGENETICS, INC. Seattle, WA 1982-1986
DNA Sequencing Group
Research Associate
Supervisor: Patrick O'Hara, Ph.D., Current position: Vice President of Biomolecular Informatics, ZymoGenetics, Inc., Seattle, WA

Was a member of the DNA Sequencing Group during which time the group grew from two people (serving a scientific staff of 15) to five people (serving a scientific staff of 50). As the assistant manager for the in-house computer, responsible for familiarizing the scientific staff with the software.

EDUCATION

BS in Cellular and Molecular Biology, supported by graduate level study in Genetics and Biochemistry
University of Washington, Seattle, WA, 1982

PUBLICATIONS

1. Lin TA, McIntyre KW, Das J, Liu C, O'Day KD, Penhallow B, Hung CY, Whitney GS, Shuster DJ, Yang X, Townsend R, Postelnek J, Spergel SH, Lin J, Moquin RV, Furch JA, Kamath AV, Zhang H, Marathe PH, Perez-Villar JJ, Doweyko A, Killar L, Dodd JH, Barrish JC, Wityak J, Kanner SB. Selective Itk inhibitors block T-cell activation and murine lung inflammation Biochemistry. 2004 Aug 31;43(34):11056-62.

2. Perez-Villar JJ, Whitney GS, Sitnick MT, Dunn RJ, Venkatesan S, O'Day K, Schieven GL, Lin TA, Kanner SB. Phosphorylation of the linker for activation of T-cells by Itk promotes recruitment of Vav. Biochemistry. 2002 Aug 27;41(34):10732-40.

3. Gena S. Whitney, Shulin Wang, Han Chang, Ke-Yi Cheng, Pin Lu, Xia D. Zhou, Wen-Pin Yang, Murray McKinnon and Malinda Longphre (2001) New Siglec Family Member, Siglec-10, is expressed in cells of the immune system and has signaling properties similar to CD33. *Eur J Biochem.* 2001 Dec;268(23):6083-96.

4. Perez-Villar, J., Whitney, G.S., Bowen, M.A., Hewgill, D.H., Aruffo, A.A., and Kanner, S.B. (1999) CD5 Negatively Regulates the T-Cell Antigen Receptor Signal Transduction Pathway:Involvement of SH2-Containing Phosphotyrosine Phosphatase SHP-1. *1999 Mol. Cell. Biol.* 19(4):2903-2912

4. Kobarg, J., Whitney, G. S., Palmer, D., Aruffo, A., and Bowen, M.A. (1997) Analysis of the tyrosine phosphorylation and signal transduction of naturally occurring human CD6 isoforms with different cytoplasmc domains. 1997 *Eur. J. Immunol.* 27(11):2971-80

5. Bowen, M.A., Bajorath, J., DÃEgidio, M., Whitney, G.S., Palmer, D., Kobarg, J., Starling, G.C., Siadak, A.W., and Aruffo, A. (1997) Characterization of mouse ALCAM (CD166): the CD6-binding domain is conserved in different homologs and mediates cross-species binding. 1997 *Eur. J. Immunol.* 27(11):2971-80

6. Starling, G.C., Llewellyn, M. C., Whitney, G.S., and Aruffo, A. (1997) The Ly-1.1 and Ly-1.2 epitopes of murine CD5 map to the membrane distal scavenger receptor cysteine-rich domain. Tissue Antigens 1997 49:1-6

7. Bowen, M.A., Whitney, G.S., Neubaurer, M., Starling, G.C., Palmer, D., Zhang, J., Nowak, N.J., Shows, T.B., and Aruffo, A. (1997). Structure and chromosomal location of the human CD6 gene:detection of five human CD6 isoforms. 1997 *J. Immunol* 158(3):1149-56

8. Bowen, M.A., Bajorath, J., Siadak, A.W., Modrell, B., Malacko, A.R., Marquardt, H., Nadler, S.G., Whitney, G., and Aruffo, A. (1996) The amino-terminal immunoglobulin-like domain of activated leukocyte cell adhesion molecule binds specifically to the membrane-proximal scavenger receptor cysteine-rich domain of CD6 with a 1:1 stoichiometry. 1996 *J. Biol. Chem.* 271(29):17390-6.

9. Starling, G.C., Whitney, G.S., Siadek, A.W., Llewellyn, M.B., Bowen, M.A., Farr, A.G. and Aruffo, A. (1996) Characterization of mouse CD6 with novel monoclonal antibodies which enhance the allogenic mixed leukocyte reaction. 1996 Eur. J. Immunol 26(4):738-46

10. Whitney,G.S., Starling G.C., Bowen, M.A, Modrell B, Siadek, A.W., and Aruffo, A. (1995) The membrane-proximal scavenger receptor cysteine-rich domain of CD6 contains the activated leukocyte cell adhesion molecule binding site. 1995 *J. Biol. Chem.* 270(31):18187-90.

11. Whitney,G.S., Bowen, M., Neubauer, M., and Aruffo, A. (1995) Cloning and characterization of murine CD6. *Mol. Immunol.* 32(1):89-92.

12. Chan, P.Y., Kanner, S.B., Whitney, G., and Aruffo, A. (1994) A transmembrane-anchored chimeric focal adhesion kinase is constitutively activated and phosphorylated at tyrosine residues identical to pp125^{FAK}. 1994 *J. Biol. Chem.* 269(32):20567-20574.

13. Whitney, G.S., Chan, P.Y., Blake, J., Cosand, W.L., Neubauer, M.G., Aruffo, A. and Kanner, S.B. (1993) Human T- and B-lymphocytes express a structurally conserved focal adhesion kinase (pp125^{FAK}). *DNA & Cell Biol.* 12:823-830.

14. Plowman, G.D., Culouscou, J.M., Whitney, G.S., Green, J.M., Carlton, G.W., Foy, L., Neubauer, M.G., and Shoyab, M. (1993) Ligand-specific activation of HER4/p180erbB4, a fourth member of the epidermal growth factor receptor family. *Proc. Natl. Acad. Sci. USA* 90(5):1746-1750.

15. Plowman, G., Whitney G.S. Neubauer, M., Green, J., McDonald, V., Todaro, G., and Shoyab, M. (1990). Molecular cloning and expression of an additional epidermal growth factor receptor-related gene. *Proc Natl. Acad. Sci. USA.* 85:55-59.

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18. DeLorenzi, M., Ali, N., Saari, G., Henry, C., Wilcox, M., and Bienz, M. (1988). Evidence that the Abdominal-B r element is conferred by a trans-regulatory homeoprotein. *EMBO J.* 7:3223-3231.

19. MacKay, V., Welch, S., Insley, M., Manney, T., Holly, J., Saari, G., and Parker, M. (1988). The Saccharomyces cervisiae BAR1 gene encodes an exported protein with homology to pepsin. *Proc. Natl. Acad. Sci. USA.* 85: 55-59.

20. Saari, G. and Bienz, M. (1987). The structure of the Ultrabithorax promoter of Drosophila melanogaster. *EMBO J.* 6:1775-1779.

21. Saari, G., Kumar, A., Kawasaki, G., Insley, M., and O'Hara, P. (1987). Sequence of the Ampullariella sp. strain 3876 gene coding for xylose isomerase. *J. Bacteriol.* 169: 612618

22. Hartig, A., Holly, J., Saari, G., and MacKay, V. (1986). Multiple regulation of the STE2, a mating-type-specific gene of Saccharomyces cervisiae. *Mol. Cell. Biol.* 6:2106-2114.

23. Ammerer, G., Hunter, C., Rothman, J., Saari, G., Valls, L., and Stevens, T. (1986). PEP4 gene of Saccharomyces cervisiae encodes proteinase A, a vacuolar enzyme required for the processing of vacuolar precursers. *Mol. Cell. Biol.* 6: 2490-2499.

24. Hagen, F., Gray, C., O'Hara, P., Grant, F., Saari, G., Woodbury, R., Hart, C., Insley, M., Kisiel, W., Kurach, K., Davie, E. (1986). Characterization of a cDNA coding for human factor VII. *Proc. Natl. Acad. Sci. USA* 83: 2412-2416.

25. McKnight, G., Kato, H., Upshall, A., Parker, M., Saari, G., O'Hara, P. (1985). Identification and molecular analysis of a third Aspergilllus nidulins alcohol dehydrogenase gene. *EMBO J.* 4: 2093-2099.